

IN THE CLAIMS

1.(currently amended) A dosage form of combination of high dose high solubility active ingredient, as modified release and low dose active ingredient as immediate release suitable for swallowing; ~~consisting essentially of micro matrix particles and coating on said micro matrix particles one or more hydrophobic release controlling agents to control the release of high dose, high solubility active ingredient, wherein said dosage form consists of~~ which comprises an inner portion having a low dose active ingredient as immediate release and an outer portion having a high dose, high solubility active ingredient as modified release, ~~in which the outer portion consists essentially of said micro matrix particles and coating on said micro matrix particles one or more hydrophobic release controlling agents~~ wherein said inner portion is covered by the outer portion from all the sides except a top surface that remains uncovered ;

wherein outer portion comprises:

a) micro matrix particles containing high dose, high solubility active ingredient and one or more hydrophobic release controlling agent wherein the ratio of high dose, high solubility active ingredient and hydrophobic release controlling agent is in the range of 100:2.5 to 100:30 and

b) a coating of one or more hydrophobic release controlling agents on said micro matrix particles, wherein the ratio of micro matrix particles and

hydrophobic release controlling agent is in the range of 100:2.5 to 100:30.

2. (canceled)

3. (canceled)

4. (previously presented) A dosage form according to claim 1, wherein the micro matrix particles comprise one or more hydrophobic release controlling agents.

5. (previously presented) A dosage form according to claim 4, wherein the hydrophobic release controlling agents are selected from the group comprising of ammonio methacrylate copolymers type A and B as described in USP, methacrylic acid copolymer type A, B and C as described in USP, polyacrylate dispersion 30% as described in Ph. Eur., polyvinyl acetate dispersion, ethylcellulose, cellulose acetate, cellulose propionate (lower, medium or higher molecular weight), cellulose acetate propionate, cellulose acetate butyrate, cellulose acetate phthalate, cellulose triacetate, poly(methyl methacrylate), poly(ethyl methacrylate), poly(butyl methacrylate), poly(isobutyl methacrylate), poly(hexyl methacrylate), poly(isodecyl methacrylate), poly(lauryl methacrylate), poly(phenyl methacrylate), poly(methyl acrylate), poly(isopropyl acrylate), poly(isobutyl acrylate), poly(octadecyl acrylate), waxes selected from the group consisting of beeswax, carnauba wax, microcrystalline wax, and ozokerite; fatty alcohols selected from the group consisting of cetostearyl alcohol, stearyl alcohol; cetyl alcohol and myristyl alcohol; and fatty acid esters selected from the group consisting of glyceryl

monostearate, glycerol distearate, glycerol monooleate, acetylated monoglycerides, tristearin, tripalmitin, cetyl esters wax, glyceryl palmitostearate, glyceryl behenate and hydrogenated castor oil.

6. (previously submitted currently amended) A dosage form according to claim 5, wherein the hydrophobic release controlling agent(s) is selected from the group consisting of ammonio methacrylate co-polymers.

7. (previously presented) A dosage form according to claim 6, wherein the ammonio methacrylate co-polymers are selected from the group consisting of Eudragit RSPO[®] (Ammonium Methacrylate Copolymer type B USP), Eudragit RL[®] (Ammonium Methacrylate Copolymer type A USP) and Eudragit NE30D[®] (Polyacrylate dispersion 30% Ph. Eur.).

8. (canceled)

9. (canceled)

10. (canceled)

11. (currently amended) A dosage form according to claim 1[[0]], wherein in micro matrix particles, the active ingredient and one or more hydrophobic release controlling agents are present in a ratio of from 100:2.5 to 100:20.

12. (previously presented) A dosage form according to claim 1, wherein said coating on said micro matrix particles comprises one or more hydrophobic release controlling agents.

13. (previously presented) A dosage form according to claim 12, wherein the hydrophobic release controlling agents are selected from the group

comprising of ammonio methacrylate copolymers type A and B as described in USP, methacrylic acid copolymer type A, B and C as described in USP, polyacrylate dispersion 30% as described in Ph. Eur., polyvinyl acetate dispersion, ethylcellulose, cellulose acetate, cellulose propionate (lower, medium or higher molecular weight), cellulose acetate propionate, cellulose acetate butyrate, cellulose acetate phthalate, cellulose triacetate, poly(methyl methacrylate), poly(ethyl methacrylate), poly(butyl methacrylate), poly(isobutyl methacrylate), poly(hexyl methacrylate), poly(isodecyl methacrylate), poly(lauryl methacrylate), poly(phenyl methacrylate), poly(methyl acrylate), poly(isopropyl acrylate), poly(isobutyl acrylate), poly(octadecyl acrylate), waxes selected from the group consisting of beeswax, carnauba wax, microcrystalline wax, and ozokerite; fatty alcohols selected from the group consisting of cetostearyl alcohol, stearyl alcohol; cetyl alcohol and myristyl alcohol; and fatty acid esters selected from the group consisting of glyceryl monostearate, glycerol distearate, glycerol monooleate, acetylated monoglycerides, tristearin, tripalmitin, cetyl esters wax, glyceryl palmitostearate, glyceryl behenate glycerol distearate, and hydrogenated castor oil.

14.(original) A dosage form according to claim 13, wherein the hydrophobic release controlling agent(s) is selected from fatty acid esters.

15.(original) A dosage form according to claim 14, wherein the hydrophobic release controlling agents is selected from the group comprising of hydrogenated castor oil and glycerol distearate.

16.(canceled)

17.(canceled)

18.(currently amended) A dosage form according to claim 1[[7]], wherein in outer portion, micro matrix particles and coating of one or more hydrophobic release controlling agents are present in a ratio of from 100:2.5 to 100:20.

19.(original) A dosage form according to claim 1, wherein the weight ratio of immediate release active ingredient and modified release active ingredient is from 1:10 to 1:15000.

20. (original) A dosage form according to claim 1, wherein the low dose active ingredient comprises dose less than or equal to 50 mg.

21.(previously presented) A dosage form according to claim 1, wherein the low dose active ingredient is selected from the group comprising of antidiabetic agents, anti-histamines, anti-depressants, anti-viral agents, anesthetics, antacids, anti-arththriics, antibiotics, anti-psychotics, anti-spasmodics, anxiolytic agents, appetite suppressants, cardiovascular agents, cough suppressants, emollients, gastro-intestinal agents,

growth regulators, respiratory stimulants, vitamins, angiotensin converting enzyme inhibitors, anti-asthmatics, anti-cholesterolemics, anti-convulsants, anti-depressants, anti-diarrhea preparations, anti-infective, anti-inflammatory agents, anti-nauseants, anti-stroke agents, anti-tumor drugs, anti-tussives, anti-uricemic drugs, amino-acid preparations, antiemetics, antiobesity drugs, antiparasitics, antipyretics, appetite stimulants, cerebral dilators, chelating agents, cholecystokinin antagonists, cognition activators, deodorants, dermatological agents, diuretics, erythropoietic drugs, fertility agents, synthetic hormones, laxatives, mineral supplements, neuroleptics, neuromuscular agents, peripheral vaso-dilators, prostaglandins, vaginal preparations, vaso-constrictors, vertigo agents, sulphonylurease, meglitinides, PPAR gamma agonist [insulin sensitisers (thiazolidinedione)], PPAR alpha and gamma agonist, and alpha-glucosidase inhibitors.

22.(currently amended) A dosage form according to claim 21, wherein the low dose active ingredient is selected from the group comprising of zafirlukast, quinapril hydrochloride, isotretinoin, rabeprazole sodium, estradiol(e2), norethindrone acetate, risedronate sodium, pioglitazone HCl, amphetamine, anagrelide hydrochloride, biperiden HCl, mephalan, alprazolam, ramipril, naratriptan hydrochloride, leflunomide, anastrozole, exemestane, paroxetine mesylate, candesartan cilexetil, almotriptan, cerivastatin, betaxolol hydrochloride, bisoprolol

fumarate, deloratadine, clonazepam, clorazepate
 dipotassium, clozapine, methylphenidate hci,
 carvedilol, warfarin sodium, norgestrel, ethinyl
 estradiol, cyclophosphamide, pemoline, liothyronine
 sodium, misoprostol, tolterodine tartrate,
 dextroamphetamine sulfate, dicyclomine
 hydrochloride, digoxin, oxybutynin chloride,
 doxazosin mesylate, ethacrynate sodium, venlafaxine
 HCl, enalapril maleate, estradiol, estropipate,
 famotidine, letrozole, fludrocortisone acetate,
 fluoxetine, dexmethylphenidate hci, alendronate
 sodium, ziprasidone, glipizide, glyburide, miglitol,
 guanabenz acetate, haloperidol, doxercalciferol,
 zalcitabine, hydrochlorothiazide, hydromorphone HCl,
 indapamide, estradiol, nitric oxide, ketorolac
 tromethamine, clonazepam, granisetron, lamotrigine,
 fluvastatin sodium, levonorgestrel, levothyroxine
 sodium, atorvastatin calcium, lisinopril, minoxidil,
 loperamide, loratidine, lorazepam, lovastatin,
 pravastatin sodium, fluvoxamine maleate,
 acetaminophen, acyclovir, aminocaproic acid,
 pitavastatin, suvastatin, dalvastatin, escitalopram,
 sertraline, elecoxib, parecoxib, valdecoxib,
 glibenclamide (glyburide), glipizide, gliclazide,
 glimepiride, tolazamide, tolbutamide, clorpropamide,
 gliquidone, nateglinide, glyburide, glisoxepid,
 glibornuride, phenbutamide, tolcyclamide,
 repaglinide, troglitazone, ciglitazone,
 pioglitazone, englitazone, acarbose, voglibose,
 emiglitate, miglitol, farglitazar, (S)-2-ethoxy-3-
 [4-(2-{4-

methanesulfonyloxyphenyl}ethoxy)phenyl]propanoic acid, 3-{4-[2-(4- tert-butoxycarbonylaminophenyl)ethoxy]phenyl}-(S)-2-ethoxy propanoic acid, L-6766892 and pharmaceutically acceptable salts thereof.

23.(currently amended) A dosage form according to claim 1, wherein the high dose, high solubility active ingredient comprises dose from 500 mg to 1500 mg.

24.(previously presented) A dosage form according to claim 1, wherein the high dose, high solubility active ingredient is selected from the group comprising of antidiabetic agents, anti-histamines, anti-depressants, anti-viral agents, anesthetics, antacids, anti-arthritis, antibiotics, anti-psychotics, anti-spasmodics, anxiolytic agents, appetite suppressants, cardiovascular agents, cough suppressants, emollients, gastro-intestinal agents, growth regulators, respiratory stimulants, vitamins, angiotensin converting enzyme inhibitors, anti-asthmatics, anti-cholesterolemics, anti-convulsants, anti-depressants, anti-diarrhea preparations, anti-infective, anti-inflammatory agents, anti-nauseants, anti-stroke agents, anti-tumor drugs, anti-tussives, anti-uricemic drugs, amino-acid preparations, antiemetics, antiobesity drugs, antiparasitics, antipyretics, appetite stimulants, cerebral dilators, chelating agents, cholecystokinin antagonists, cognition activators, deodorants, dermatological agents, diuretics, erythropoietic drugs, fertility agents, synthetic hormones, laxatives, mineral

supplements, neuroleptics, neuromuscular agents, peripheral vaso-dilators, prostaglandins, vaginal preparations, vaso-constrictors, biguanides, and vertigo agents.

25.(original) A dosage form according to claim 1, wherein the high dose, high solubility active ingredient is selected from the group comprising of metformin hydrochloride, phenformin, buformin, potassium chloride, clindamycin, hydroxyurea, erythromycin, lactobionate, vancomycin hydrochloride, balsalazide disodium, sodium valproate, niacin, aminocaproic acid, acetaminophen ciprofloxacin, quetiapine and pharmaceutically acceptable salts thereof.

26.(original) A dosage form according to claim 1, wherein inner portion may optionally contain more than one low dose active ingredients.

27.(original) A dosage form according to claim 1, wherein the dissolution of high dose, high solubility active ingredient is not more than 45% in 1 hour and between 25% to 90% in 6 hours.

28.(canceled)

29.(canceled).

30.(previously presented) A process for the preparation of a dosage form as claimed in claim 1, comprising a) preparation of inner portion and b) preparation of outer portion.

31.(original) A process for the preparation of a dosage form as claimed in claim 30, wherein preparation of outer portion comprising a) preparing a micro matrix particles containing high dose, high solubility active ingredient and one or more hydrophobic release controlling agent and b) coating the said micro matrix particles containing high solubility active ingredient and one or more hydrophobic release controlling agent.

32.(original) A dosage form according to claim 1, wherein outer portion may optionally contain more than one high dose high solubility active ingredients.

33. (currently amended) A dosage form of combination of high dose high solubility antidiabetic active ingredient ~~[[is]]~~ as modified release and low dose antidiabetic active ingredient as immediate release, suitable for swallowing; ~~comprising micromatrix particles and coating on said micromatrix particles to control the release of the high dose high solubility antidiabetic active ingredient wherein said dosage form comprising of~~ which comprises an inner portion having a low dose antidiabetic active ingredient as immediate release and an outer portion having a high dose, high solubility antidiabetic active ingredient as modified release, wherein said inner portion is covered by the outer portion from all the sides except a top surface that remains uncovered; ~~in which~~ wherein the outer portion comprises

a) ~~said~~ micro matrix particles containing high dose, high solubility antidiabetic active ingredient and one or more hydrophobic release controlling agent wherein the ratio of high dose, high solubility antidiabetic active ingredient and hydrophobic release controlling agent is in the range of 100:2.5 to 100:30

and b) a coating of one or more hydrophobic release controlling agents on said micro matrix particles, wherein the ratio of micro matrix particles and hydrophobic release controlling agent is in the range of 100:2.5 to 100:30 ~~on said micro matrix particles and the inner portion is covered by the outer portion from all the sides except top surface that remains uncovered.~~

34. (canceled)

35. (canceled)

36. (previously presented) A dosage form according to claim 33, wherein the micro matrix particles comprise one or more hydrophobic release controlling agents.

37. (previously presented) A dosage form according to claim 36, wherein the hydrophobic release controlling agents are selected from the group comprising of ammonium methacrylate copolymers type A and B as described in USP, methacrylic acid copolymer type A, B and C as described in USP, polyacrylate dispersion 30% as described in Ph. Eur., polyvinyl acetate dispersion, ethylcellulose, cellulose acetate, cellulose propionate (lower,

medium or higher molecular weight), cellulose acetate propionate, cellulose acetate butyrate, cellulose acetate phthalate, cellulose triacetate, poly(methyl methacrylate), poly(ethyl methacrylate), poly(butyl methacrylate), poly(isobutyl methacrylate), poly(hexyl methacrylate), poly(isodecyl methacrylate), poly(lauryl methacrylate), poly(phenyl methacrylate), poly(methyl acrylate), poly(isopropyl acrylate), poly(isobutyl acrylate), poly(octadecyl acrylate), waxes selected from the group consisting of beeswax, carnauba wax, microcrystalline wax, and ozokerite; fatty alcohols selected from the group consisting of cetostearyl alcohol, stearyl alcohol; cetyl alcohol and myristyl alcohol; and fatty acid esters selected from the group consisting of glyceryl monostearate; glycerol monooleate, acetylated monoglycerides, tristearin, tripalmitin, cetyl esters wax, glyceryl palmitostearate, glyceryl behenate, glycerol distearate and hydrogenated castor oil.

38. (previously presented) A dosage form according to claim 37, wherein the hydrophobic release controlling agent(s) is selected from the group consisting of ammonio methacrylate co-polymers.

39. (previously presented) A dosage form according to claim 38, wherein the ammonio methacrylate co-polymers are selected from the group consisting of Eudragit RSPO® (Ammonium Methacrylate Copolymer type B USP), Eudragit RL® (Ammonium Methacrylate

Copolymer type A USP) and Eudragit NE30D® (Polyacrylate dispersion 30% Ph. Eur.).

40. (canceled)

41. (canceled)

42. (canceled)

43. (currently amended) A dosage form according to claim [[42]] 33, wherein in micro matrix particles, the antidiabetic active ingredient and one or more hydrophobic release controlling agents are present in a ratio of from 100:2.5 to 100:20.

44. (canceled)

45. (currently amended) A dosage form according to claim 33[[44]], wherein coating on micro matrix comprises one or more hydrophobic release controlling agents wherein the hydrophobic release controlling agents are selected from the group comprising of ammonio methacrylate copolymers type A and B as described in USP, methacrylic acid copolymer type A, B and C as described in USP, polyacrylate dispersion 30% as described in Ph. Eur., polyvinyl acetate dispersion, ethylcellulose, cellulose acetate, cellulose propionate (lower, medium or higher molecular weight), cellulose acetate propionate, cellulose acetate butyrate, cellulose acetate phthalate, cellulose triacetate, poly(methyl methacrylate), poly(ethyl methacrylate), poly(butyl methacrylate), poly(isobutyl methacrylate), poly(hexyl methacrylate), poly(isodecyl methacrylate), poly(lauryl methacrylate), poly(phenyl methacrylate),

poly (methyl acrylate), poly (isopropyl acrylate), poly (isobutyl acrylate), poly (octadecyl acrylate), waxes selected from the group consisting of beeswax, carnauba wax, microcrystalline wax, and ozokerite; fatty alcohols selected from the group consisting of cetostearyl alcohol, stearyl alcohol; cetyl alcohol and myristyl alcohol; and fatty acid esters selected from the group consisting of glyceryl monostearate; glycerol monooleate, acetylated monoglycerides, tristearin, tripalmitin, cetyl esters wax, glyceryl palmitostearate, glyceryl behenate, glycerol distearate and hydrogenated castor oil.

46. (previously presented) A dosage form according to claim 45, wherein the hydrophobic release controlling agent(s) is selected from fatty acid esters.

47. (original) A dosage form according to claim 46, wherein the hydrophobic release controlling agents are selected from the group comprising of hydrogenated castor oil and glycerol distearate.

48. (canceled)

49. (canceled)

50. (currently amended) A dosage form according to claim [[49]] 33, wherein in outer portion, micro matrix particles and coating of one or more hydrophobic release controlling agents are present in a ratio of from 100:2.5 to 100:20.

51. (original) A dosage form according to claim 33, wherein the weight ratio of immediate release

antidiabetic active ingredient and modified release antidiabetic active ingredient is from 1:10 to 1:15000

52. (original) A dosage form according to claim 33, wherein the low dose antidiabetic active ingredient comprises dose less than or equal to 50 mg.

53. (original) A dosage form according to claim 33, wherein the low dose antidiabetic active ingredient is selected from the group comprising of sulphonylurease, meglitinides, PPAR gamma agonist[insulin sensitisers (thiazolidinedione)], alpha-glucosidase inhibitors, PPAR alpha and gamma agonist.

54. (currently amended) A dosage form according to claim 33, wherein the low dose antidiabetic active ingredient is selected from the group comprising of glibenclamide (glyburide), glipizide, gliclazide, glimepiride, tolazamide, tolbutamide, clorpropamide, gliquidone, nateglinide, glyburide, glisoxepid, glibornuride, phenbutamide, tolcyclamide, repaglinide, troglitazone, ciglitazone, pioglitazone, englitazone, acarbose, voglibose, emiglitate, miglitol, farglitazar, (S)-2-ethoxy-3-[4-(2-{4-methanesulfonyloxyphenyl}ethoxy)phenyl]propanoic acid, 3-{4-[2-(4-tert-butoxycarbonylamino)phenyl]ethoxy}phenyl)-(S)-2-ethoxy propanoic acid and pharmaceutically acceptable salts thereof.

55. (original) dosage form according to claim 33, wherein the high dose high solubility antidiabetic active ingredient is selected from biguanides.

56. (original) A dosage form according to claim 33, wherein the high dose high solubility antidiabetic active ingredient is selected from the group comprising of metformin hydrochloride, phenformin and buformin

57. (original) A dosage form according to claim 33, wherein the high dose high solubility antidiabetic active ingredient comprises dose from 500 mg to 1500 mg.

58. (original) A dosage form according to claim 33, is once a day oral formulation.

59. (original) A dosage form according to claim 33, is used for human beings.

60. (original) A dosage form according to claim 33, wherein the high dose high solubility antidiabetic active ingredient is metformin hydrochloride.

61. (previously presented) A dosage form according to claim 60, wherein the composition of outer portion is as follows-

Micro matrix particles-

Metformin hydrochloride 75%w/w to 99%w/w

Eudragit RS® 1%w/w to 25%w/w

Coated micro matrix particles

Micro matrix particles 70%w/w to 99%w/w
Hydrogenated castor oil 1%w/w to 30%w/w
Magnesium stearate 0%w/w to 2%w/w

62. (previously presented) A dosage form according to claim 60, wherein the dissolution of metformin hydrochloride is not more than 50% in one hour, from 30 to 90 % in four hours and not less than 65 % in twelve hours.

63. (previously presented) A dosage form according to claim 60, wherein the maximum plasma metformin concentration is achieved between 700 ng/ml and 2500 ng/ml.

64. (previously presented) A dosage form according to claim 63, wherein the maximum plasma metformin concentration is achieved between 900 ng/ml and 2400 ng/ml.

65. (previously presented) A dosage form according to claim 63, wherein the maximum plasma metformin concentration is achieved between 1000 ng/ml and 2350 ng/ml.

66. (previously presented) A dosage form according to claim 60, wherein the modified release metformin hydrochloride formulations for once daily administration exhibit in vivo mean dissolution time (MDT) of 4 hours to 6 hours.

67. (previously presented) A dosage form according to claim 60, wherein the minimum plasma metformin concentration (at 24 hours) ranges between 0 and 450 ng/ml after oral administration.
68. (original) A dosage form according to claim 33, wherein the low dose antidiabetic active ingredient is rosiglitazone maleate.
69. (original) A dosage form according to claim 33, wherein the low dose antidiabetic active ingredient is glimepiride.
70. (previously presented) A dosage form as claimed in claim 60 or 68, wherein the bioavailability of rosiglitazone is not affected when it is coadministered with metformin hydrochloride.
71. (original) A dosage form according to claim 33, wherein inner portion may optionally contain more than one antidiabetic active ingredients.
72. (original) A dosage form according to claim 33, wherein outer portion may optionally contain more than one antidiabetic active ingredients.
73. (withdrawn) A process for the preparation of a dosage form as claimed in claim 33, comprising a) preparation of inner portion and b) preparation of outer portion.

74. (withdrawn) A process for the preparation of a dosage form as claimed in claim 73, wherein preparation of outer portion comprising a) preparing a micro matrix particles containing high dose, antidiabetic active ingredient and one or more hydrophobic release controlling agent and b) coating the said micro matrix particles containing high dose antidiabetic active ingredient and one or more hydrophobic release controlling agent.